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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/905,558 | 07/13/2001 | Carl W. Garnaat | 1016 | 2761 |

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| EXAMINER | |
|---|---|
| IBRAHIM, MEDINA AHMED | |
| **ART UNIT** | **PAPER NUMBER** |
| 1638 | 16 |

DATE MAILED: 03/12/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application N . | Applicant(s) | |
|---|---|---|---|
| | 09/905,558 | GARNAAT ET AL. | |
| | Examiner | Art Unit | |
| | Medina A Ibrahim | 1638 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *30 January 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☐ Claim(s) *1-36* is/are pending in the application.

4a) Of the above claim(s) *1-14 and 33-36* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *15-32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *13 July 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *3, 13* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

## DETAILED ACTION

### *Election/Restrictions*

1. Applicant's election with traverse of Group III claims 15-32 in Paper No. 12 is acknowledged. The traversal is on the ground(s) that restriction requirement between SEQ ID NO: 3, 4, and 16 is improper because the three sequences share structural similarity of 99% as shown in the attached sequence alignment. Applicant further argued that the sequences differ only in a single nucleotide at position 776 and 1306-1307. Applicant urges that the restriction requirement between SEQ ID NO: 3, 4, and 16 be withdrawn. Applicants further argue that the restriction requirement between the primers of claim 15, part (e) is improper because all 5 primers are designed for the amplification of a single gene. Applicant urges that the restriction requirement between SEQ ID NO: 6, 7, 8, 9, and 10 be withdrawn. Applicant's arguments have been fully considered but not all are persuasive.

Applicants' argument regarding the primers is found persuasive, and therefore, SEQ ID NO: 6, 7, 8, 9, and 10 will be examined together in this application. However, Applicant's arguments against the restriction requirement between SEQ ID NO: 3, 4, and 16 are not persuasive because Applicant has not shown that the single nucleotide difference between the sequences is obvious over each other. Absent such showing or a statement from the Applicant saying that SEQ ID NO: 3, 4, and 16 are not patentably distinct; the restriction requirement may be maintained. Therefore, the requirement is still deemed proper and is therefore made FINAL.

Claims 1-36 are pending. Claims 15-32 and SEQ ID NO: 16 are under examination. Claims 1-14 and 33-36 and SEQ ID NO: 1, 3-5 are withdrawn from consideration as being drawn to the non-elected invention.

***Sequence Listing***

Applicant's CRF and paper sequence listing have been entered.

***Drawings***

The drawings filed with this application are approved by the Examiner.

***Specification***

1. The disclosure is objected to because of the following informalities: for example page 18, line 9, and page 52, line 23, cite a hyperlink directed to an Internet address. The use of hyperlinks is not permitted under USPTO current policy because the content of such links are subject to a change, resulting in the introduction of New Matter into the specification. Appropriate correction is required.

***Claim Objections***

Claim 15 is objected to because of the following informalities: the claim recites a non-elected invention. The claim should be amended accordingly. In claim 18, "an expression cassette" lacks the proper article. It is suggested that "an" is replaced with --the---.

***Claim Rejections - 35 USC § 112***

2. The following is a quotation of the **second paragraph** of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 15-32 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

4. In claim15, part (b), it is unclear what is intended by "operable fragments". Dependent claims 16-32 are included in the rejection. Also, part (e), without any active, positive steps delimiting how this use is actually practiced.

Claim 20 is indefinite for failing to recite a proper Markush group.

In claim 21, "disruption of plant fertility" is unclear. It is unclear whether "disruption" means reduction, loss, or something else

Claim 32 is indefinite for lacking agreement between the preamble and method steps.

***Claim Rejections - 35 USC § 112***

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 13 and 21 rejected under 35 U.S.C. 112, **first paragraph**, because the specification, while being enabling for an isolated polynucleotide comprising SEQ ID NO: 16 having transcriptional regulatory activity responsive to auxin, a recombinant expression cassette comprising said polynucleotide operably linked to an encoding polynucleotide of interest, transgenic plants and seed comprising said recombinant expression cassette, and a method of altering expression of Ms45 gene to affect plant fertility, does not reasonably provide enablement for any isolated polynucleotide having

at least 75% sequence identity with SEQ ID NO:16, operable fragments thereof, polynucleotides amplified from *Zea mays* nucleic acids library using specified primers, and nucleic acids from the 5' regulatory region of any polynucleotide having 75% sequence identity to *ZmAxig1* coding region, a polynucleotides which selectively hybridizes to said polynucleotides under specified stringent conditions, and still having transcriptional regulatory activity, transgenic plants and seeds comprising said polynucleotides, and a method of altering plant gene expression or disrupting plant fertility by expressing said polynucleotides in transgenic plants. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The claims are broadly drawn to any isolated polynucleotide having at least 75% sequence identity with SEQ ID NO: 16, operable fragments thereof, polynucleotides amplified from *Zea mays* nucleic acids library, and nucleic acids from the 5' regulatory region of any polynucleotide having 75% sequence identity to *ZmAxig1* coding region, and polynucleotides which selectively hybridizes to said polynucleotides under stringent conditions, having transcriptional regulatory activity. The claims are also drawn to, transgenic monocot and dicot plants and seeds comprising said polynucleotides, and a method of expressing said polynucleotides in plants to affect plant fertility.

Applicant provides guidance for isolated promoter sequences from the 5' region of the auxin-induced polynucleotide from Zea mays designated as *ZmAxig1* including transcriptional regulatory elements of said polynucleotide. Applicant also provided

guidance for the construction of two recombinant vectors, V1 comprising the *ZmAxig 1* promoter comprising 661 base pairs operably linked to the coding sequence of the Ms45 gene, and V2 construct comprising components similar to V1 except that it has the full-length *ZmAxig promoter*. Transformation of maize embryos was carried out using the two vectors (Example 3). The *ZmAxig 1* promoters were shown to drive the anther-specific expression of the Ms45 in maize cells in the presence of auxin. Transgenic plants and progeny with altered fertility as a result of the expressing said recombinant polynucleotides have also been disclosed (Example 4).

Applicant has not provided guidance for how to obtain all of the polynucleotides of claims 15 and 16 and use them for the production of transgenic plants with altered fertility. No guidance has been provided for any modifications to any of the disclosed sequences that results in a polynucleotide having at least 75% sequence identity with any of the disclosed sequences, operable fragments, or polynucleotides, other than *ZmAxig 1,* amplified from *Zea mays* nucleic acids library or from the 5' regulatory region of any polynucleotide having 75% sequence identity to *ZmAxig1* coding region, and polynucleotides which selectively hybridize to said polynucleotides under stringent conditions, and having auxin responsive regulatory activity. No regions necessary for auxin-responsive regulatory activity have been disclosed or evaluated for these polynucleotides. Applicant has not provided guidance as to what modifications would allow the disclosed sequences to retain their regulatory activity, so as heterologous genes can be expressed to provide the desired male sterility/fertility trait in transgenic

plants. In addition, No transgenic plant with altered gene expression or altered phenotype as a result of expressing said modified polynucleotides have been disclosed.

The state of the art teaches unpredictability inherent in promoters to function either constitutively or tissue-specifically when one or more nucleotide bases of the promoter are modified. For example, Kim et al (Plant Molecular Biology, 1994 vol. 24, pp. 105-117) teach the extreme sensitivity of promoter regions to single base pair changes, the absolute requirement for as few as 3 to 6 nucleotides for promoter function, and the failure of a promoter to function either constitutively or specifically when lacking oligonucleotide regions approximately 100 bp upstream of the transcription start site (page 106, paragraph bridging the columns; paragraph bridging pages 107 and 108; page 110, paragraph bridging the columns). Benfey et al (Science, 1990, vol. 250, pages 959-966) teach tissue specificity of fragments of the CaMV 35S promoter can vary depending on the location of the fragment within a promoter (Figure 1, page 960). In addition, the claimed hybridizing sequences, and sequences having 75% sequence identity would comprise non- functional transcriptional, translational, elements, i.e. modifications to highly conserved promoter regions such as CAAT, and TATA elements, required for proper expression of genes, may be rendered inactive by said modifications. Therefore, the ability of the claimed polynucleotides to function as promoter is uncertain.

While Applicant is not required to exemplify each and every claimed embodiment, specific guidance with respect to which region of the disclosed sequences can be modified so that the auxin-responsive regulatory activity is retained is required.

Absent such guidance, one skilled in the art would not be able to make the polynucleotides as broadly claimed to provide proper expression of heterologous proteins in transgenic plants, without undue experimentation.

Therefore, given the lack of guidance as discussed supra; the unpredictability inherent in the function of a promoter when lacking specific regions necessary for regulatory activity, the breadth of the claims; and state of the art, the claimed invention is not enabled.

See *Amgen Inc. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ 2d 1016 at 1027 (Fed. Cir. 1991), where it is taught that the disclosure of a single gene sequence did not enable claims broadly drawn to any analog thereof.

***Written Description***

Claims 15-32 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are broadly drawn to any isolated polynucleotide having at least 75% sequence identity with SEQ ID NO: 16, operable fragments thereof, polynucleotides amplified from *Zea mays* nucleic acids library using specified primers, and nucleic acids from the 5' regulatory region of any polynucleotide having 75% sequence identity to *ZmAxig1* coding region, a polynucleotide which selectively hybridizes to said polynucleotides under specified stringent conditions, and having transcriptional regulatory activity responsive to auxin. The claims are also drawn to a recombinant

expression cassette, transgenic plants and seeds comprising said polynucleotides, and a method of altering plant gene expression or fertility of transgenic plants.

The claimed invention does not meet the current written description requirements for the following reasons: Firstly, Applicant has not described a single variant having the claimed structural characteristics that retains the desired regulatory activity. Secondly, Applicant has not described the auxin responsive regulatory elements in the disclosed sequences. Applicant has only described promoter sequences from the *ZmAxig 1* polynucleotide, transgenic plants and seeds comprising them, and a method for expressing a desired gene under the control of said promoter in transgenic plants. Applicant fails to describe the composition and structure of other nucleic acid sequences encompassed by the claims. In particular, Applicant has not described all polynucleotides having at least 75% sequence identity with SEQ ID NO: 16, operable fragments thereof, all polynucleotides having 75% sequence identity to *ZmAxig1* coding region, all polynucleotides which selectively hybridize to the disclosed polynucleotides and having auxin-responsive regulatory activity. Consequently, Applicant fails to provide an adequate written description for expression vectors, plants, plant cells and seed comprising said sequences, and for methods for using said sequences to express a desired gene in transgenic plants, as claimed in claims 17-32.

See *University of California v. Eli Lilly and Co.* 43 USPQ2d 1398 (Fed. Cir. 1997), where the court stated:

"A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the

scope of the genus or of a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus". See, also Written description Examination Guidelines published in Federal Registry/Vol. 66, No.4/Friday, January 5, 2001/Notices).

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

3. Claims 15, 17-22, 25-28 and 30-32 are rejected under 35 U.S.C. 102(b) as being anticipated by Cigan et al (US 5, 795, 753, Filed June 1995).

The claims are broadly drawn to an isolated polynucleotide having at least 75% sequence identity with SEQ ID NO: 16, operable fragments thereof, polynucleotides amplified from *Zea mays* nucleic acids library using specified primers, and nucleic acids from the 5' regulatory region of any polynucleotide having 75% sequence identity to *ZmAxig1* coding region, a polynucleotide which selectively hybridizes to said polynucleotides under specified stringent conditions, and having transcriptional regulatory activity responsive to auxin. The claims are also drawn to recombinant expression cassette, anther-specific promoter, monocot and dicot transgenic plants and seeds comprising said polynucleotides, and a method of altering plant fertility/sterility by affecting expression of Ms45 gene in said transgenic plants, and a plant breeding method.

Cigan et al teach a genetic construct comprising an isolated anther-specific promoter of 5126 gene from maize operably linked to a gene encoding a product that inhibits pollen formation, transformed maize plants and seed comprising said genetic construct, and a method for producing male sterile plant by expressing said construct in a transgenic plant, in the absence of auxin. Application of auxin to said transformed plant results in male fertile plant. The reference also teaches breeding the transformed with another plant of the same species. Given the broad interpretations of "operable fragments", the 5126 gene promoter from maize would inherently comprise an operable fragment of Applicant's SEQ ID NO: 16. Therefore, Cigan teaches all claim limitations.

***Remarks***

The polynucleotide sequence of SEQ ID NO: 16 is deemed free from prior art of record.

No claim is allowed.

Papers related to this application may be submitted to Technology Sector 1 by facsimile transmission. Papers should be faxed to Crystal Mall 1, Art Unit 1638, using fax number (703) 308-4242. All Technology Sector 1 fax machines are available to receive transmission 24 hrs/day, 7 days/wk. Please note that the faxing of such papers must conform with the Notice published in the Official Gazette, 1096 OG 30 (November 15, 1989).

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Medina A. Ibrahim whose telephone number is (703) 306-5822. The Examiner can normally be reached Monday-Thursday from 8:30AM to 5:30PM and every other Friday 9:00AM to 5:00PM.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Dr. Amy Nelson, can be reached at (703) 306-3218.

Any inquiry of a general nature or relating to the status of this application should be directed to the receptionist whose telephone number is (703) 308-0196.

1/22/03
Mai

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